UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/579,135	04/11/2007	Ifor Delme Bowen	000487.00042	6308

22907 7590 05/29/2009

BANNER & WITCOFF, LTD.
1100 13th STREET, N.W.
SUITE 1200
WASHINGTON, DC 20005-4051

EXAMINER	
MI, QIUWEN	

ART UNIT	PAPER NUMBER
1655	

MAIL DATE	DELIVERY MODE
05/29/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/579,135	BOWEN ET AL.	
	Examiner	Art Unit	
	QIUWEN MI	1655	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 March 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2-9 and 11* is/are pending in the application.

4a) Of the above claim(s) *3,6,7 and 9* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2,4,5,8 and 11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *15 May 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5/15/06; 4/11/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Claims 2-9, and 11 are pending.

Applicant's election of Group I, claims 2-5, 8, and 11 (newly added, drawn to elected invention Group I), and species gamma-bisabolene and leukemia, in the reply filed on 3/19/09 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 3, 6, 7, and 9 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim.

Since elected species leukemia was not found in the art, search was extended to breast cancer.

Claims 1 and 10 are cancelled.

Claims 2, 4, 5, 8, and 11 are examined on the merits.

Specification/Abstract Objections

Applicant is reminded of the proper language and format for an abstract of the disclosure.

The abstract should be in narrative form and generally limited to a single paragraph on a separate sheet within the range of 50 to 150 words. It is important that the abstract not exceed 150 words in length since the space provided for the abstract on the computer tape used by the printer is limited. The form and legal phraseology often used in patent claims, such as "means" and "said," should be avoided. The abstract should describe the disclosure sufficiently to assist readers in deciding whether there is a need for consulting the full patent text for details.

The language should be clear and concise and should not repeat information given in the title. It should avoid using phrases which can be implied, such as, "The disclosure concerns," "The disclosure defined by this invention," "The disclosure describes," etc.

In the instant case, Applicant is required to delete "The present invention relates to" on line 1, and "The present invention also relates to" on lines 1-2 of the Abstract to be more clear and concise. The first letter of "the" in line 1, the first "a" in line 2 should be capitalized after the deletion.

Claim Rejection 112, 1st

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 2, 4, 5, 8, and 11 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating cancer by administering to a patient in need thereof an effective dose of gamma-bisabolene, does not reasonably provide enablement for preventing cancer in a subject with the claimed compound. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in In re Wands, 8 USPQ2d 1400 (Fed. Cir. 1988). Among these factors are: (1) the nature or the invention; (2) the breadth of the claims; (3) the state of the prior art; (4) the relative skill of those in the art; (5) the predictability or unpredictability of the art; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

When the above factors are weighed, it is the examiner's position that one skilled in the art could not practice the invention without undue experimentation.

(1) The nature of the invention:

The invention is drawn to a method for treating or preventing cancer comprising administering to a patient in need of such treatment an effective dose of a compound, wherein the compound is a terpene or oxygenated derivative thereof, and the terpene is selected from the group consisting of trans-beta-ocimene; and gamma-risabolene.

In regards to "preventing a cancers", Merck manual indicates that cancer is an unregulated proliferation of cells due to loss of normal controls, resulting in unregulated growth, lack of differentiation, local tissue invasion, and often, metastasis. Cancer can develop in any tissue or organ at any age (see "Introduction to Cancer" from Merck Manual, pp. 1, accessed on 3/5/08).

Tomatis (Tomatis, Environmental cancer risk factors, Acta oncologica (Stockholm, Sweden), (1988) Vol. 27, No. 5, pp. 465-72. Ref: 31) teaches the risk of cancer in humans is increased by a wide spectrum of factors, which ranges from exposure to an identified agent, such as environmental chemicals or a virus, to a culturally determined behaviour, such as smoking, or to socio-economic conditions.

Merck manual indicates that some families have a significantly higher risk of developing certain cancers. Sometimes the increased risk is due to a single gene and sometimes it is due to several genes interacting together. Environmental factors—common to the family—may alter this genetic interaction and produce cancer. Numerous environmental factors increase the risk of developing cancer. Tobacco smoke contains carcinogens that substantially increase the risk of

developing cancers of the lungs, mouth, throat, esophagus, kidneys, and bladder. Pollution in the air, whether from industrial waste or cigarette smoke, can increase the cancer risk. Many chemicals are known to cause cancer, and many others are suspected of doing so. For example, asbestos exposure may cause lung cancer and mesothelioma (cancer of the pleura), especially in smokers. Exposure to pesticides is associated with a higher risk of some types of cancer (for example, leukemia and non-Hodgkin lymphoma). The time between exposure to the chemicals and development of the cancer may be many years. Exposure to radiation is a risk factor in the development of cancer. Extended exposure to ultraviolet radiation, primarily from sunlight, causes skin cancer. Ionizing radiation is particularly carcinogenic. Exposure to the radioactive gas radon, which is released from soil, increases the risk of lung cancer. Normally, radon disperses rapidly into the atmosphere and produces no harm. However, when a building is placed on soil with a high radon content, radon can accumulate within the building, sometimes producing sufficiently high levels in the air to cause harm. Radon is breathed into the lungs, where it may eventually cause lung cancer. In exposed people who also smoke, the risk of lung cancer is further increased (see "risk factor for cancer" from Merck Manual, pp. 1-4, accessed on 4/14/09).

(2) the breadth of the claims:

The invention is drawn to a method for treating or preventing cancer comprising administering to a patient in need of such treatment an effective dose of a compound, wherein the compound is a terpene or oxygenated derivative thereof, and the terpene is selected from the group consisting of trans-beta-ocimene; and gamma-risabolene. Thus, the breadth of the claims encompasses that by administering to a subject gamma-risabolene, the incidence of developing

cancer is reduced to zero. Regardless whether the person has family history of cancer, with mutation of caner related genes, or how the person exposes to tobacco smoke, asbestos, pesticides, or ultraviolet radiation, with the administration of gamma-risabolene, it would prevent cancer from ever happening.

(3) the state of the art:

However, the claimed method is contradicting from the findings of the prior art. Tomatis teaches it would be impossible to have just one simple approach to cancer control and cancer prevention (see Abstract). Kronborg (Kronborg, Population screening for colorectal cancer, the goals and means, Annals of medicine, (1991 Oct) Vol. 23, No. 4, pp. 373-9) teaches that the causes of colorectal cancer are complex and in most cases obscure, making primary prevention impossible at present (see Abstract). Garewal et al (Garewal et al, Clinical experience with the micronucleus assay, Journal of Cellular Biochemistry, (1993) Vol. 52, No. SUPPL. 17 F, pp. 206-212) teach because of the logistical and practical problems that make cancer prevention trials using cancer incidence as an endpoint virtually impossible to conduct for the majority of cancer types, there is a desperate need for valid intermediate markers of cancer risk to serve as surrogate endpoints in chemoprevention trials (see Abstract). Cheng et al (Cheng et al, A novel approach to microcalcification detection using fuzzy logic technique, IEEE transactions on medical imaging, (1998 Jun) Vol. 17, No. 3, pp. 442-50) teach since the cause of breast cancer remains unknown, primary prevention becomes impossible (see Abstract).

Therefore, preventing cancer from ever happening is currently not attainable.

(4) the relative skill of those in the art

The relative skill in the art is high. The level of a person of ordinary skill in the art is high, with ordinary artisans having advanced medical and/or scientific degrees (e.g.M.D., Ph.D., Pharm. D. or combinations thereof).

(5) The predictability or unpredictability of the art:

The prevention of cancer is highly unpredictable. The majority of studies suggest that the essential element towards the validation of a preventive therapeutic is the ability to test the drug on subjects monitored in *advance* of clinical cancer and *link* those results with subsequent histological confirmation of the presence or absence of disease. This irrefutable link between antecedent drug and subsequent knowledge of the prevention of the disease is the essence of a valid preventive agent. Further, a preventive administration also must assume that the therapeutic will be safe and tolerable for anyone susceptible to the disease. Further more, such studies require the appropriate experimental models for analyzing chemo-or immunoprevention. For example, Granziero *et al.* (Granziero *et al.* Adoptive immunotherapy prevents prostate cancer in a transgenic animal model, Eur. J. Immunol. 1999, 29:1127-1138) teach that many models are not suitable for testing immunotherapeutic approaches intended to cure cancer. They suggest that the optimal model (prostate cancer, in their case) would have spontaneous tumor development in its natural location (1st column, page 1128) wherein disease progression would closely resemble the progression of the particular type of cancer. Hence, depending on the type of model employed one could establish a reasonable link between antecedent drug and subsequent knowledge of the prevention of the disease. Further, reasonable guidance with respect to correlating agents that prevent cancer may depend upon quantitative analysis from defined populations that have been successfully pre-screened and are predisposed to particular types of

cancer. This type of data might be derived from widespread genetic analysis, cancer clusters, or family histories. For example, Byers, T. (Byers, T, What can randomized controlled trials tellus about nutrition and cancer prevention, CA Journal, Vol. 49, No. 6, Nov/Dec. 1999) teaches that randomized controlled trials are commonly regarded as the definitive study for proving causality (1st col., p. 358), and that in controlled trials the random assignment of subjects to the intervention eliminates the problems of dietary recalls and controls the effects of both known and unknown confounding factors. Further, Byers suggests that chemo-preventitive trials be designed "long-term" such that testing occurs over many years (2nd CO1. p. 359). The specification is devoid of any models or experimental analysis that reasonably suggests that the claimed method would predictably prevent the formation of cancer in a patient. This, combined with the state of the art of preventing cancer, suggests that undue experimentation would be required to practice the invention as broadly claimed.

Since preventing cancer is such a complex issue, the state of the art has not been able to prevent cancer from happening. In addition, none of the claimed compound has been able to reduce the incidence of cancer to zero, thus the predictability of the art is very low.

(6) The amount of direction or guidance presented.

The specification has not provided guidance on prevention cancer by using the claimed method.

Regarding cancer treatment, the specification provides cytotoxicity data of ethanol extract of C. molmol, trans-beta-ocimene, gamma-bisabolene, and alpha-bisabolol in cancer cell lines S180, HT1080, MM6, A375 and apoptotic effect of ethanol extract of C. molmol using Annexin V binding assay.

(7) The presence or absence of working examples.

There is no working example regarding how to prevent cancer.

Regarding cancer treatment, the specification provides examples regarding cytotoxicity data of ethanol extract of C. molmol, trans-beta-ocimene, gamma-bisabolene, and alpha-bisabolol in cancer cell lines S180, HT1080, MM6, A375 and apoptotic effect of ethanol extract of C. molmol using Annexin V binding assay.

(8) The quantity of experimentation necessary:

Since preventing cancer is such a complex issue, the state of the art has not been able to prevent cancer from happening. Plus none of the claimed compound has been able to reduce the incidence of cancer to zero, and the specification has not provided any guidance regarding how to prevent cancer using any of the claimed compound, the quantity of experimentation is undue. Further more, in order to prevent cancer, the treatment regimen must be identified, and the end point of the prevention also needs to be identified. Since the Applicant have not provided the appropriate time frame at which the compound should be administered to prevent cancer, one of ordinary skill in the art would be burdened with undue "painstaking experimentation study" to determine if the compound would be effective in preventing cancer.

Based on the aforementioned reasons the Examiner concludes that the specification, while being enabling for the treatment of cancer, does not reasonably provide enablement for the prevention of cancer without requiring the ordinary skilled artisan to undertake undue experimentation. Since the state of the art is highly unpredictable and requires much greater guidance for an ordinary skilled artisan to effectively prevent cancer.

Burdensome experimentation, such as clinical studies would necessarily be required of the ordinary skilled artisan to establish the prevention of cancer.

Claim Rejections –35 USC § 112, 2nd

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 2, 4, 5, 8, and 11 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 2 recites "terpene or oxygenated derivative" in line 3. The phrase "terpene or oxygenated derivative" is unclear. It is unclear what modifications of the terpene would be encompassed in the terpene or oxygenated derivative. The terpene or oxygenated derivative can be any structure, or any modification. Thus, it is unclear what modifications and derivatives are encompassed by the claimed terpene or oxygenated derivative.

Therefore, the metes and bounds of claims are rendered vague and indefinite. The lack of clarity renders the claims very confusing and ambiguous since the resulting claims do not clearly set forth the metes and bounds of the patent protection desired.

All other cited claims depend directly or indirectly from rejected claims and are, therefore, also, rejected under U.S.C. 112, second paragraph for the reasons set forth above.

Claim Rejections –35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 2, 4, 5, and 8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cohen (WO 02/080951 A1), in view of Squires (US 6,350,784 B1).

Cohen teaches herbal extracts for the treatment of cancer (see Title). Cohen states it is further a particularly presently preferred aspect of this invention that the extract used to treat a patient are obtained from the herb species Commiphora myrrha, Vaccaria segetalis etc. The solid tumor cancer being treated is an epithelial cell cancer in another aspect of this invention. The epithelial cell cancer is breast or ovarian cancer (page 3, lines 3-13). Cohen also teaches a method for treating a solid tumor cancer, comprising administering to a patient in need thereof a therapeutically effective amount of a composition comprising an extract of one or more of Commiphora myrrha etc (claim 5), wherein the extract is an alcohol extract (claim 13), and wherein the alcohol is ethyl alcohol (claim 14).

Cohen does not teach the claimed concentration of the compound.

As evidenced by Squires, Commophora myrrha contains phytochemical gamma-bisabolene (see claim 1, lines 58-65).

Therefore, when a therapeutically effective amount of extract of Commiphora myrrha is being administered to a patient who is having cancer as taught by Cohen, compound gamma-bisabolene is being administered to the patient too.

It would have been *prima facie* obvious for one of ordinary skill in the art at the time the invention was made to treat cancer using the extract of Commiphora myrrha as Cohen teaches Commiphora myrrha as one of the preferred extracts to treat cancer. Since Cohen yielded beneficial results in cancer treatment, one of ordinary skill in the art would have been motivated to use the invention. Regarding the claimed concentration of the extract or the compound, the result-effective adjustment in conventional working parameters is deemed merely a matter of judicious selection and routine optimization which is well within the purview of the skilled artisan, which is dependent upon the age, weight, cancer stage of the patient, and also the frequency of the administration and the plant extraction method. It has been held that where the general conditions of a claim are disclosed in the prior art, discovering the optimum or workable ranges involves only routine skill in the art. The differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955). (Claimed process which was performed at a temperature between 40°C and 80°C and an acid concentration between 25% and 70% was held to be prima facie obvious over a reference process which differed from the claims only in that the reference process was performed at a temperature of 100°C and an acid concentration of 10%.); see also Peterson, 315 F.3d at 1330, 65 USPQ2d at 1382 ("The normal desire of scientists or artisans to improve upon what is already generally known provides the motivation to determine where in a disclosed set of percentage ranges is the optimum

combination of percentages."); In re Hoeschele, 406 F.2d 1403, 160 USPQ 809 (CCPA 1969) (Claimed elastomeric polyurethanes which fell within the broad scope of the references were held to be unpatentable thereover because, among other reasons, there was no evidence of the criticality of the claimed ranges of molecular weight or molar proportions.). For more recent cases applying this principle, see Merck & Co. Inc. v. Biocraft Laboratories Inc., 874 F.2d 804, 10 USPQ2d 1843 (Fed. Cir.), cert. denied, 493 U.S. 975 (1989); In re Kulling, 897 F.2d 1147, 14 USPQ2d 1056 (Fed. Cir. 1990); and In re Geisler, 116 F.3d 1465, 43 USPQ2d 1362 (Fed. Cir. 1997). see MPEP § 2144.05 part II A. Although the prior art did not specifically disclose the claimed concentration of the component, it would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to determine all operable and optimal concentrations of components because concentrations of the claimed components are art-recognized result effective variables because they have the ability to treat cancer, which would have been routinely determined and optimized in the pharmaceutical art.

From the teachings of the references, it is apparent that one of the ordinary skills in the art would have had a reasonable expectation of success in producing the claimed invention.

Thus, the invention as a whole is *prima facie* obvious over the references, especially in the absence of evidence to the contrary.

Conclusion

No claim is allowed.

Claim 11 is free of art.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Qiuwen Mi whose telephone number is 571-272-5984. The examiner can normally be reached on 8 to 5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Terry McKelvey can be reached on 571-272-0775. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Qiuwen Mi/

Examiner, Art Unit 1655